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Lung function testing in the elderly—Can we still use $FEV_1/FVC < 70\%$ as a criterion of COPD?

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KEYWORDS
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Summary
Background: Chronic obstructive pulmonary disease (COPD) can be diagnosed when the FEV_1/FVC ratio is below 70%, according to global initiative for chronic obstructive lung disease (GOLD). COPD is known as a disease which is frequently under-diagnosed. However, there is a risk of over diagnosis when this diagnostic threshold is applied among the elderly.
Aims: To contribute to the discussion about the criteria for diagnosing COPD, by describing lung function and pulmonary symptoms in a population aged 60 years or more, and in particular the changes in the mean and 5% percentile of the FEV_1/FVC ratio by increasing age.
Methods: A cross sectional population-based study was performed in the city of Tromsø, Norway, in 2001–2002. Spirometry was performed in 4102 people 60 years and older (54.6% women), who also filled in a questionnaire.
Results: Decreased FEV_1% predicted and FEV_1/FVC ratio were associated with smoking, increasing age, and reported pulmonary and cardiovascular diseases. Dyspnoea and coughing were also strongly associated with smoking and reported pulmonary and cardiovascular diseases, but coughing did not become more frequent by increasing age. In never smokers aged 60–69 years the frequency of FEV_1/FVC ratio $<70\%$ was approximately 7% compared to 16–18% in those 70 years or more ($p<0.001$). FEV_1/FVC ratio $<70\%$ among never smokers aged 60–69 years was just as frequent as FEV_1/FVC ratio $<65\%$ in never smokers older than 70 years.
Conclusion: Adjustments of the GOLD criteria for diagnosing COPD are needed, and FEV_1/FVC ratios down to 65% should be regarded as normal when aged 70 years and older.

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Introduction

Chronic obstructive lung disease (COPD) is increasing in the whole world, and it is estimated to be the third leading cause of death, and the fifth leading cause of disability in the world within 20–50 years.[1–3] Smoking is responsible for the majority of cases,[1,4,5] and due to the cumulative effect of years of smoking, the prevalence of COPD increases with age.[6]

Spirometry is recommended in the diagnosis and evaluation of COPD,[1,7,8] and Global initiative for chronic obstructive lung disease (GOLD) has defined COPD to be present when the FEV_1/FVC ratio is below 70%.[1] Also ATS-ERS and NICE guidelines use $FEV_1/FVC \leqslant 70\%$ post-bronchodilator as a criterion for diagnosing COPD, regardless of age.[9] It is, however, well known that the FEV_1/FVC ratio decreases with increasing age,[6] and that the use of a fixed ratio for all ages may lead to misclassifications, under diagnosis in the younger population and over diagnosis among the elderly.[7,10–13] To contribute to the decision on valid cut-off points for the FEV_1/FVC ratio in the diagnosis of COPD, we have studied lung function and pulmonary symptoms in a general population aged 60 years or more.

Methods

Subjects

The survey took place in Tromsø, a city in the northern part of Norway with about 61 000 inhabitants, and 7842 inhabitants aged 60 years or more (January 2001). There is little occupational or environmental pollution in Tromsø.

This fifth cross sectional ''Tromsø Study'' was conducted by The University of Tromsø in cooperation with the National Health Screening Service. It started March 2001 and ended February 2002.

In the fourth survey in 1994, all citizens aged 25 years or more (37 558 persons) were invited to a brief examination. Those who were 55–74 years of age, and a random sample of 5–10% of the others between 25–84 years, were also asked to take part in a second, more detailed medical examination (phase 2); 7965 persons (77%) met. All the phase 2 participants from the fourth survey, who still lived in Tromsø, were eligible to participate in the two phases of the fifth study, and met twice with a few weeks gap. In addition all inhabitants aged 60 and 75 years were invited. In subjects aged 60 years and above, a total of 5328 subjects were eligible and 4713 (88.5%) attended phase one, and 4519 (85%) attended also phase two. Spirometry was included for the first time in the Tromsø Study, and was performed in 4102 subjects, 90% of the attendees and 77% of the eligible for participation. Absence of staff and technical problems were reasons for spirometry not being performed in 10% of the attendees.

Examinations

A questionnaire including smoking habits and different symptoms and diseases, were sent by mail together with the invitation to participate. Spirometry was carried out with the use of one spirometer only, a ''Sensormedics Vmax 20''. The American Thoracic Society-criteria for spirometry testing[14] were followed. Calibration of the instrument was performed every morning and on the machines demand. Three trained technicians shared the conducting of the spirometry. The subjects were sitting, using a nose clip, and were instructed to blow as long as possible, and at least for 6 s. The participants took a full inspiration before inserting the mouthpiece (''open circuit''). At least three exhalations where required. The difference between best and next best FEV_1 and FVC should not exceed 5% or 200 ml, whichever was the greater. Reversibility test was not performed. Current drug therapy was not interrupted before the test. Height was measured barefoot.

Quality test

In week 41 and 42 in 2001 an inter- and intra observer agreement test was done with two of our three technicians (A and B) and 80 participants. It implied repeated testing both weeks. The two technicians were blinded for each other's results.

Statistical analysis

Spirometric results and symptoms were analysed according to sex, age, smoking habits and reported lung and cardiovascular disease. Those who reported to be never smokers, and not having asthma, bronchitis, angina pectoris, myocardial infarction or stroke, were classified as healthy never smokers. FEV_1% predicted and FVC% predicted were calculated based on the Norwegian equation developed by Langhammer and co-workers.[15] Linear regression models and independent samples T-tests, and Chi-square test were used to check whether differences between groups were statistically significant. The mean and the 5% percentile of FEV_1/FVC% in healthy never smokers were compared with the expected mean and lower limit of normal (LLN = the estimated 5% percentile) according to an equation developed by Enright and co-workers.[7] Inter- and intra-observer agreement were evaluated in 2×2 tables with $FEV_1/FVC \geqslant 70\%$ as threshold, using Kappa statistics and Bland–Altman plots. The SPSS 14.0 for Windows (SPSS inc, Chicago, Illinois, USA) was used in the statistical analyses.

The Regional Committee for Medical Research Ethics approved the study. All the participants gave informed written consent.

Results

Spirometry was performed in 4102 persons aged 60 years or more, 2269 women and 1833 men. At the completion of the data collection, 25 women and 12 men had withdrawn their consent to participate. Ninety women and 21 men (2.7% of all) were excluded due to inadequate performance (of these 84 women and 20 men blew less than 3 s). The 62 women and 12 men who exhaled 3–6 s (where FVC did not exceed FEV_6), were included in the analysis, which in total comprised of 2154 women aged 60–89 and 1800 men aged 60–85 years (Table 1). Significantly more women (46%) than men (18%) were never smokers ($p < 0.001$) (Table 1 and 2). Asthma and

Table 1 Characteristics of the participants in the study.

	Women		Men	
	n	%	*n*	%
Total	2154	54.5	1800	45.5
Age (years)				
60–64	598	27.7	434	24.1
65–69	554	25.7	523	29.0
70–74	507	23.6	442	24.6
75–79	382	17.7	306	17.0
80+	113	5.2	95	5.3
Smoking habit[a]				
Never smoker	999	46.9	327	18.3
Ex-smoker	633	29.7	1043	58.3
Current smoker	498	23.4	419	23.4
Pack-years smoked[b]				
<10	401	42.2	331	26.4
10–19	275	29.0	377	30.1
20–29	185	19.7	270	21.5
30+	85	9.1	275	22.0
Reported diseases				
Cardiovascular	325	15.1	491	27.3
Myocardial Infarction	109	5.1	264	14.7
Cerebral Stroke	87	4.0	110	6.1
Angina	214	9.9	283	15.7
Pulmonary	303	14.1	219	12.2
Asthma	233	10.8	158	8.8
Chronic Bronchitis	133	6.2	98	5.4

[a]Missing data in 23 women and 11 men.
[b]Missing data in 185 women and 209 men.

Table 2 Smoking habits in the participants.

	Never smokers	Previous smokers	Current smokers
Women (all)	($n = 999$)	($n = 633$)	($n = 498$)
	46.4	29.4	23.1
60–69 years	42.9	29.2	27.0
70 years or more	50.9	29.6	18.7
Men (all) ($n = 1043$)	($n = 327$) ($n = 419$)		
	18.2	57.9	23.3
60–69 years	20.7	53.2	25.6
70 years or more	15.3	63.3	20.6

Numbers given in %.
Missing in 23 women and 11 men.

bronchitis were reported in 14.1% women and 12.2% men ($p = 0.053$), whilst cardiovascular diseases were reported by 15.1% women and 27.3% men ($p < 0.001$).

In women mean FEV_1% predicted was almost identical in all age groups, and FVC% predicted was above 90 regardless of age and smoking status, except for current smokers (Table 2). In men the FEV_1% predicted and FVC% predicted decreased significantly both by increasing age and by smoking habit ($p < 0.001$, Table 3). The FEV_1/FVC ratio decreased significantly by increasing age in both sexes ($p < 0.001$).

All the three lung function measures were significantly lower in both sexes when chronic pulmonary disease was reported than in those who neither reported pulmonary nor cardiovascular disease ($p < 0.001$, Table 2). Reporting cardiovascular disease was significantly associated with reduced lung function in men ($p < 0.001$), while only FEV_1% predicted ($p = 0.009$) and FVC% predicted ($p = 0.003$) were reduced in women with such diseases (Table 3).

Dyspnoea when walking slowly on level ground was reported more frequently by women than by men, but only significantly in those with pulmonary diseases ($p = 0.004$, Table 4). Daily coughing in periods of the year was reported more frequently in men than in women ($p < 0.001$), and was especially increased in smokers and those who reported asthma or chronic bronchitis. This symptom was, however, reported by more than 10% of healthy never smokers (Table 4).

The frequency of FEV_1/FVC ratio <70% increased by increasing age in both sexes, irrespective of smoking habits (Table 5). A fifteen-fold higher frequency was found among current smoking men aged 70 years or more (61.5%) than among healthy never smoking men aged 60–69 years (3.9%). In never smokers aged 60–69 years the frequency of FEV_1/FVC ratio <70% was approximately 7%, compared to 16–18% in those 70 years or more ($p < 0.001$). FEV_1/FVC ratio <70% among never smokers aged 60–69 years was just as frequent as FEV_1/FVC ratio <65% in never smokers older than 70 years. When applying a FEV_1/FVC limit of 65% among those above 70 years of age, the prevalence of COPD would be reduced from 26.2 to 13.2% in all women, and from 38.1 to 20.5% in all men (Tables 5 and 6). The prevalence of cough and dyspnoea were inversely correlated with lung function in the oldest age group (Table 7).

Among the healthy never smoking women, the mean FEV_1/FVC ratio fell from 78.4% in the 60–64 years age group, to 71.4% among those aged 80 years or more (Fig. 1). The fall was somewhat steeper than expected from Enright's equations. The corresponding numbers for men were 78.9% and 74.7%, and the mean FEV_1/FVC ratio was higher than expected from this equation (Fig. 2). The 5% percentile of the FEV_1/FVC ratio also dropped more steeply among the women than expected from the Enright equations (Fig. 3), and was about 65% in women aged 70 years or more, and 60% in women older than 80 years. Similar results were found among the men, but these are less valid due to a lower number of subjects (Fig. 4).

The inter-observer and intra-observer agreement in measuring FEV_1/FVC higher or lower than 70%, showed Kappa values in the range 0.77–0.92 (mean 85.5). Three out of four Kappa values were above 0.80 both in those aged 60–69 years (mean 0.85) and those who were older (mean 0.83). The Bland–Altman plots were homogenous, and are shown in Fig. 5.

Table 3 Spirometric results in 2154 women and 1800 men by age groups, smoking status, reported diseases, and for the healthy never smokers.

	Women				Men			
	n	FEV_1% predicted Mean	FVC% predicted Mean	FEV_1/FVC (%) Mean	*n*	FEV_1% predicted Mean	FVC% predicted Mean	FEV_1/FVC (%) Mean
All	2154	84.5	91.3	74.0	1800	81.4	89.6	72.4
Age groups								
60–65	598	84.9	91.2	75.4	434	85.7	92.0	74.8
65–69	554	84.2	90.8	74.5	532	82.7	90.6	73.0
70–74	507	84.7	91.8	73.4	442	80.1	89.2	71.3
75–79	382	84.1	91.3	72.4	306	76.7	86.1	70.5
80+	113	85.4	92.8	71.9	95	75.5	85.5	69.4
Smoking habit								
Never smoker	994	88.0	92.9	75.7	327	87.0	91.5	76.0
Ex-smoker	629	84.7	91.6	73.8	1035	81.8	89.4	72.8
Current smoker	498	77.3	87.9	70.5	417	76.3	88.6	68.7
Reported cardiovascular diseases								
Myocardial infarction	109	81.2	88.3	73.3	261	74.6	83.8	70.9
Cerebral stroke	87	80.2	86.1	74.5	108	75.1	84.4	70.7
Angina pectoris	214	81.8	88.0	74.2	283	76.8	85.9	71.1
Reported pulmonary disease								
Asthma	233	71.5	82.4	68.8	157	66.1	81.0	64.8
Chronic bronchitis	133	69.0	81.1	67.4	97	66.3	80.1	64.7
Healthy never smokers	730	89.6	94.3	76.0	235	89.3	92.8	77.8

The Norwegian A. Langhammer reference values are used.

Discussion

The study confirms what is known from previous epidemiological surveys[7,11,12,16–18] that the FEV_1/FVC ratio falls significantly after the age of 60. $FEV_1/FVC < 70\%$ was 50% more frequent in women older than 70 years compared to those aged 60–69 years (26.2% and 17.4%, respectively, Table 5). The corresponding increase in men was 80%. The relative increase was much higher among healthy never smokers, approximately 170% in both sexes, than among current smokers, 30% in women and 60% in men. Does this increase in the frequency of $FEV_1/FVC < 70\%$ among healthy never smokers by increasing age reflect an increasing prevalence of COPD, or mainly the normal ageing process?

To be a smoker is the most important reason for getting COPD.[1] In our material women aged 70 years or more were 8.0% more frequently never smokers and 8.3% less frequently current smokers than those who were in the sixties (Table 2). In men, current smokers also became less frequent by increasing age. One may question whether there really is an increase in the prevalence of COPD by increasing age, particularly in women.

Only small differences occurred in reported cough and dyspnoea between subjects under and over 70 years of age, except for dyspnoea on walking slowly on level ground ($p < 0.001$ women and $p = 0.005$ men, Table 4). The tendency of less coughing in the oldest age group among women may also indicate that the prevalence of COPD did not increase.

The reduction in lung function can to some degree be explained by the structural changes that take place in the airways with increasing age, including dilatation of the alveoli and loss of supportive tissue in the peripheral airways called "senile emphysema".[13] Another aspect of normal ageing is loss of muscular tissue generally and reduced physical endurance. The elderly suffer, in addition, from other diseases, co-morbidities which may influence the lung function.[7] Heart failure, in particular, is known to be associated with reduced spirometric values, including the FEV_1/FVC ratio in severe cases.[19]

Table 4 Reported symptoms in women and men by age-groups, smoking habits and reported diseases.

	Women				Men			
	Dyspnoea on slow walking[a]	Dyspnoea on quick walking[b]	Cough daily in periods[c]	Chronic cough[d]	Dyspnoea on slow walking[a]	Dyspnoea on quick walking[b]	Cough daily in periods[c]	Chronic cough[d]
All	4.1	48.5	16.1	10.7	3.1	46.3	22.6	14.5
Age groups								
60–69	3.5	47.2	16.5	10.7	2.6	45.1	22.0	13.8
70+	5.7	51.1	14.6	10.4	4.3	48.5	23.3	15.9
Smoking habit								
Never smoker	4.1	45.7	12.3	8.4	1.5	33.3	15.0	9.8
Ex-smoker	3.9	50.7	13.6	9.8	3.0	47.3	17.8	11.6
Current smoker	4.2	51.4	26.9	16.9	4.3	53.7	40.3	25.1
Reporting cardiovascular diseases	8.9	70.5	15.4	10.5	7.5	64.0	22.6	14.9
Reporting pulmonary disease	11.9	71.3	41.3	29.7	4.6	69.4	46.1	35.6
Healthy never smokers	2.1	37.8	10.4	7.1	1.3	28.1	12.3	8.1

Numbers given in %.
[a]Dyspnoea when walking slowly on level ground.
[b]Dyspnoea when walking quickly on level ground or slightly upwards.
[c]Daily coughing in periods of the year.
[d]Coughing more than three months during the last 2 years.

Table 5 Prevalence (%) of $FEV_1/FVC < 70\%$ by age and smoking habits in women and men.

	Healthy never smokers	Never smokers	Previous smokers	Current smokers	All
Women					
60–69 years	6.2	7.0	17.0	35.0	17.4
70 years or more	16.8	18.0	28.0	46.0	26.2
Men					
60–69 years	3.9	7.6	18.3	37.1	21.1
70 years or more	10.8	16.3	35.2	61.5	38.1

Table 6 Prevalence (%) of $FEV_1/FVC < 65\%$ in those 70 years and older, by age and smoking habits in women and men.

	Prevalence (%) of $FEV_1/FVC < 65\%$				
	Healthy never smokers	Never smokers	Previous smokers	Current smokers	All
Women					
70 years or more $FEV_1/FVC < 65\%$	4.9	6.7	13.5	31.0	13.2
Men					
70 years or more $FEV_1/FVC < 65\%$	2.4	7.8	17.8	37.4	20.5

Table 7 Prevalence (%) of reported symptoms by FEV_1/FVC in women and men above 70 years of age.

	n	Dyspnoea on slow walking[a]	Dyspnoea on quick walking[b]	Cough daily in periods[c]	Chronic cough[d]
FEV_1/FVC					
<65%	305	8.9	65.6	32.8	25.2
65–69%	279	6.1	54.8	23.3	13.3
70% or more	1261	3.9	45.0	14.0	9.8

[a]Dyspnoea when walking slowly on level ground.
[b]Dyspnoea when walking quickly on level ground or slightly upwards.
[c]Daily coughing in periods of the year.
[d]Coughing more than three months during the last 2 years.

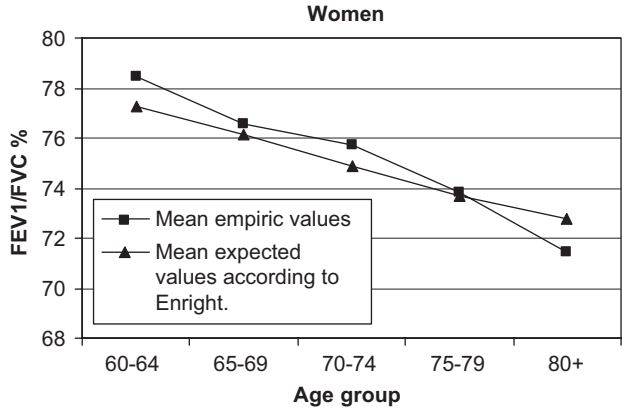

Figure 1 Mean FEV_1/FVC ratios in 730 never smoking women, without reported pulmonary or cardiovascular disease (healthy never smokers), by age group, compared with expected values according to the reference equations of Enright.

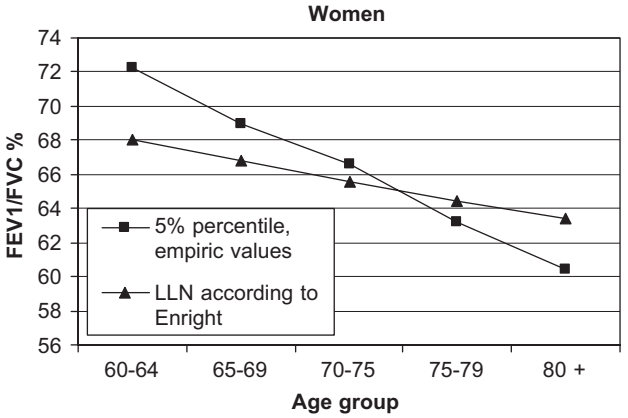

Figure 3 The 5% percentile of FEV_1/FVC in 730 never smoking women, without reported pulmonary or cardiovascular disease (healthy never smokers), by age group, compared with expected LLN (lower limit of the normal range = fifth percentile) values according to the reference equations of Enright.

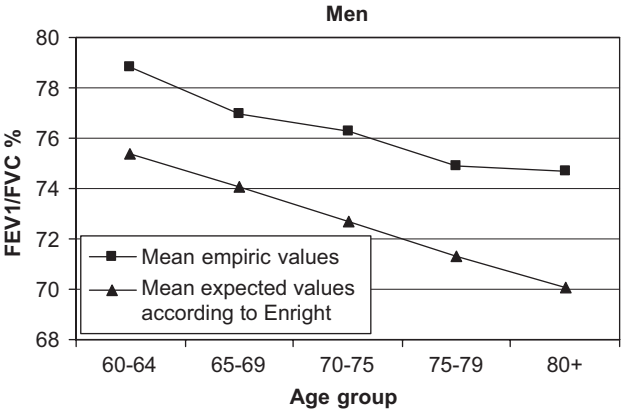

Figure 2 Mean FEV_1/FVC ratios in 235 never smoking men, without reported pulmonary or cardiovascular disease (healthy never smokers), by age group, compared with expected values according to the reference equations of Enright.

COPD is certainly under-diagnosed in the society. Johannessen and co-workers found that only 43% of subjects with COPD had been diagnosed by a doctor, and the majority of these had a GOLD stage 2–3 COPD.[20] Only 5% of those classified as having GOLD stage 1 ($FEV_1/FVC<70\%$ and $FEV_1>80\%$ predicted) had been diagnosed in the health care system as having COPD in a Swedish survey.[21] Cautions should be made in classifying persons fulfilling GOLD stage 1 criteria as having COPD. The clinical importance of GOLD stage 1 has been questioned by a recent study, in which no increased risk of death was associated with such a mild degree of "COPD".[22]

It seems obvious that we need a lower spirometric threshold when diagnosing COPD in the elderly. A threshold of 65% after the age of 70 can be suggested on the basis of our results (Table 6, Figs. 3 and 4). The tendency of lower frequency of "COPD" among the oldest age group of healthy never smokers (which was not statistically significant) can probably be explained by a "healthy survivor" effect.[23] A fixed ratio used as a threshold in a large age group can never be more than "a rule of the thumb". Comparison with a LLN (lower limit of normal) age-related curve may be a good alternative, in order to improve the diagnostic precision. However, diagnostic thresholds will always be arbitrary and other explanations than COPD should always be considered when a borderline result or moderate obstruction is found. New thresholds should be evaluated against clinical usefulness.

It is important to avoid medicalisation.[24] Many elderly people use five to 10 types of medicines already. Over diagnosis of COPD may lead to unnecessary use of pulmonary medication, and an additional diagnosis could increase their feeling of being unfit.

The results are probably representative of the elderly population in Tromsø. The attendant rate in phase 2 was 85% and the 10% who did not perform a spirometry due to technical problems and absence of staff were not subject to selection bias. There may be some bias in our material because we did not invite non-participants from earlier studies. We have information on responders and non-responders to a questionnaire that was handed out at the screening in an earlier Tromsø survey.[25] The subjects who returned the questionnaire tended to be married, non-smoking, and reporting respiratory symptoms less often than non-responders. The non-responders did otherwise not vary much from the responders. A mortality follow-up study of persons invited to a cardiovascular disease survey in five areas in Norway, has shown a mortality rate 3.7 times higher (age-adjusted all-cause mortality rate) in non-attending women and a 2.2 times higher mortality rate in non-attending men compared to attendees.[26] Our results might therefore be a little higher than in the total population.

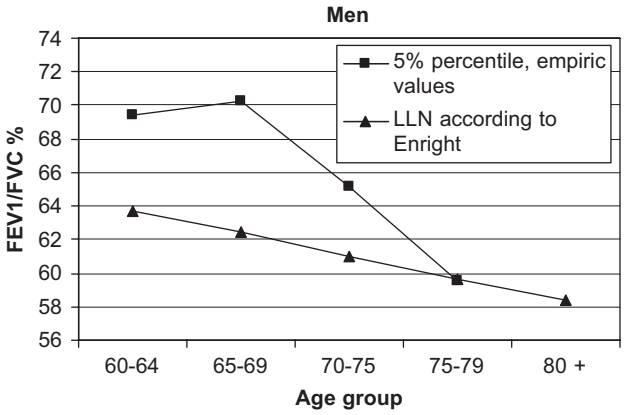

Figure 4 The 5% percentile of FEV_1/FVC in 235 never smoking men, without reported pulmonary or cardiovascular disease (healthy never smokers), by age group, compared with expected LLN (lower limit of the normal range = fifth percentile) values according to the reference equations of Enright. Estimation could not be made in those older than 80 years, due to a low number of subjects ($n = 14$).

The mean FVC% predicted did not reach 100%, not even in healthy never smokers. When using the equation from European Community for Steele and Coal,[14] the mean FVC% predicted were 107% and 98% in women and men, respectively. The inclusion criterions to the reference material of Langhammer et al.[15] are strict, not allowing any reported respiratory symptoms like wheezing and breathlessness during the last 12 months. Only 236 never smokers older than 60 years were included. The reference values may be too strict for our elderly population.

We are confident with the quality of the spirometry. There were only three technicians involved, and only one spirometer was used. The Kappa-values for the inter- and intra-observer agreements were close to optimal and the

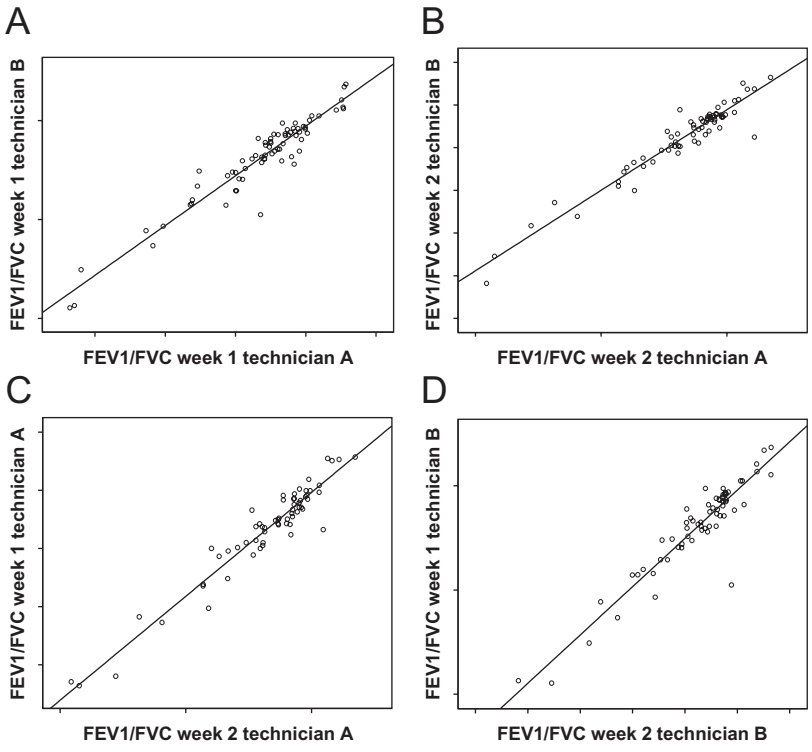

Figure 5 Bland-Altman plots of inter- and intra observer variability test of $FEV_1/FVC < 70\%$ for two technicians in two subsequent weeks. (A) FEV_1/FVC week 1.Technician A versus technician B. (B) FEV_1/FVC week 2.Technician A versus technician B. (C) FEV_1/FVC week 1 versus week 2 for technician A. (D) FEV_1/FVC week 1 versus week 2 for technician B.

Bland–Altman plots are homogenous (Fig. 5). The 74 subjects, who blew for more than three, but less than 6 s, were included in the analyses. Excluding these subjects induced only minimal and insignificant changes of the results.

Higher FEV_1/FVC% values were found among the healthy never smoking men than expected on the basis of Enright's material (Fig. 2). One reason for this may be the less strict inclusion criterions in Enright's study, as people who had smoked up to five pack-years also were included.

The omission of reversibility testing is a weakness of our study. Johannessen et al. found that the prevalence of FEV_1/FVC below 70% decreased by approximately 18% after inhalation of a beta2-agonist for subjects 60 years and over,[27] and our spirometric values would probably have been somewhat higher if they had been based on reversibility testing. However, the frequency in our study of FEV_1/FVC ratio less than 70% among subject 75–79 years was similar to the frequencies found by Lundbäck et al.[28] after reversibility testing in subjects aged 76–77 years, both in smokers and never smokers. The negative effect of not doing reversibility testing may to some degree have been reduced by the fact that on-going medication, including anti-asthma medicines, had not been interrupted.

The FEV_1/FVC ratio is a practical indicator of the lung function. It is easily measured, and can be used without the need of reference equations. The application of the 70% threshold in all ages is, however, an oversimplification, as previously stated by Enright, Falaschetti and Hardie.[7,11,12] Adjustments have to be done to make the measure clinically useful and credible. A threshold of 65% after the age of 70 can be suggested on the basis of our results.

Acknowledgements

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